REMARKS

Claims 18, 29, 43 and 44 are canceled without prejudice or disclaimer. Applicants reserve the right to file a continuation or divisional application or take such other action to preserve their rights to the subject matter canceled by claim cancellation or amendment.

Claim 12 is amended to incorporate formula **1** from canceled claim 18, and to recite substituents for alkyl and aryl groups supported, for example, at page 7, lines 1-11. Also, the definition of R^1 and R^2 is amended to include "hydroxy, alkoxy, aryloxy, heteroaryloxy, ...amino, alkylamino, dialkylamino, acylamino, ... alkylthio, arylthio, acylthio, ... alkylsulfonyl, arylsulfonyl" as supported in the specification, for example, at page 11, lines 15-21. The definition of R^1 and R^2 is also amended to provide that the compound of formula 13 is a primary or secondary amine, which is supported, for example, at page 5, lines 23-25.

Claim 12 is also amended to recite that the combinatorial library comprises the compounds as: a mixture; an array having each compound located at a different position at a substrate, at least one of the compounds being coupled to the substrate through R^1 or R^2; or a set of sub pools of the compounds, wherein within each sub pool the compounds are prepared from the same amine represented by formula **13**, the same carbonyl represented by formula **14**, or the same organoborane represented by formula **15** or formula **19**. Support is provided in the specification, for example, at page 7, lines 14-36.

Likewise, claims 19-21 are amended to recite that the combinatorial library comprises the compounds as the set of the sub pools of the compounds (claim 19), the mixture of the compounds (claim 20) and the array of the compounds (claim 21).

Claim 12 is also amended to make the recitation of the preparation of the compounds more consistent and definite.

Claim 35 is amended to recite "at least one of the compounds is present in diasteromeric excess or enantiomeric excess." Likewise, claim 36 is amended to recite specific percentages of diasteromeric or enantiomeric excess. Support for these amendments is provided, for example, at page 6, lines 5-12.

Various typographical amendments have been made throughout the claims.

Rejection under 35 U.S.C. § 102 (b)/103(a) re Palfreyman et al.

The Examiner maintains the rejection of combinatorial library claims 12, 18-21, 29, 35-39, 43, and 44 under 35 U.S.C. § 102 (b) as anticipated by, or, in the alternative, under 35 U.S.C. § 103 (a) as obvious over Palfreyman *et al.* U.S. Pat. No. 4,421,767 ("the '767 patent"). The '767 patent describes compounds of formulas I, II, and III which can be administered either alone or in combination with an aromatic L-amino acid decarboxylase inhibitor for the treatment of depression. The Examiner states that the '767 patent discloses a collection of individual pure compounds.

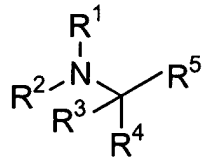
Applicants have canceled claims 18, 29, 43 and 44, and have amended claim 12 to specify the form of the library. Thus, by contrast to the '767 patent, the claims are drawn (claim 12) to a combinatorial library comprising a plurality of compounds that includes the compounds as: a mixture; an array having each compound located at a different position at a substrate, at least one of the compounds being coupled to the substrate through R^1 or R^2; or a set of sub-pools of the compounds, wherein the compounds within each sub pool are prepared from the same amine represented by formula **13**, the same carbonyl represented by formula **14**,or the same organoborane represented by formula **15** or formula **19**.

Therefore, the '767 patent does not anticipate the claimed combinatorial library because it does not describe each and every element as set forth in claim 12, nor does it suggest the presently claimed combinatorial library. Withdrawal of the corresponding rejections under 35 U.S.C. § 102 (b) and 35 U.S.C. § 103 (a) is respectfully requested.

Rejection under 35 U.S.C. § 102 (b)/103(a) re Kick *et al.*

The Examiner rejects claims 12, 18-21, 29, 35-39, 43, and 44 under 35 U.S.C. § 102 (b) as anticipated by, or, in the alternative, under 35 U.S.C. § 103 (a) as obvious over Kick *et al.*, J. Med Chem. 1995, 38, 1427-1430. The Office Action states that compounds 7a, 7b, and 7c of the Kick *et al.* reference read directly on instant formula **1** where R^1, R^3, and R^4 are hydrogen, R^2 is carboxamido, and R^5 is heteroaryl.

Applicants have canceled claims 18, 29, 43 and 44, and have amended claim 12 to recite that the plurality of compounds in the combinatorial library are represented by formula **1**.



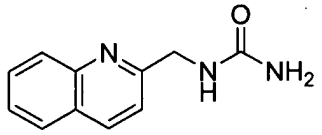
1

Claim 12 requires that R^1 and R^2, are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, hydroxy, alkoxy, aryloxy, heteroaryloxy, acyl, acylalkyl, carboxy, , amino, alkylamino, dialkylamino, acylamino, carboxamido, alkylthio, arylthio, acylthio, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, phosphinyl, alkylsulfonyl, arylsulfonyl, and -YR, where Y is selected from the group consisting of -O-, -NR_a-, -S-, -SO-, and -SO_2-, and R and R_a are each independently selected from the group consisting of hydrogen, alkyl, aryl, heteroaryl, and acyl, or R^1 and R^2 together form a methylene bridge of 2 to 20 carbon atoms, provided that the compound of formula 13 is a primary or secondary amine. Moreover, each alkyl is optionally substituted with one or more groups selected from the group consisting of C1-C6 alkyl, C3-C6 heterocycle, aryl, halo, hydroxyl, alkoxy, and sulfonyl; and each aryl is optionally substituted with aryl or lower alkyl.

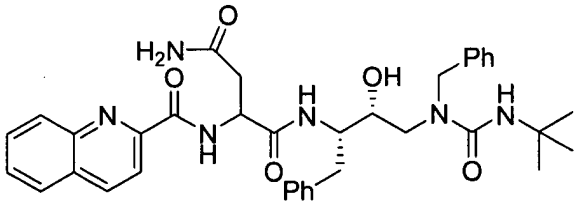
By contrast, none of the compounds disclosed in the Kick *et al.* reference are encompassed by formula **1**. No nitrogen atom in compounds 7a-7i in the Kick *et al.* reference can correspond to the substituted N atom shown in formula **1**. Each nitrogen atom in the compounds of the Kick *et al.* reference is either aromatic; a terminal amide; an N_3 group; incorporated in a morpholine, substituted piperidine or substituted piperizine ring; or has a

substituent not permitted by R^1 and R^2 in formula **1** such as quinolinyl-CO-, substituted carboxamido, quinolinyl-CONH-substituted acyl, or tetrahydrofuryl carboxy ester.

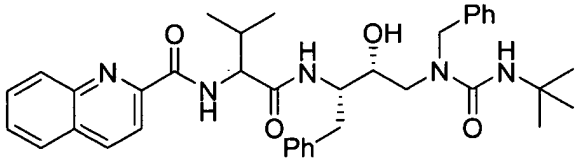
More particularly, contrary to the statement in the Office Action, compounds 7a, 7b, and 7c of the Kick *et al.* reference do not read on formula **1** of the instant claims when R^1, R^3, and R^4 are hydrogen, R^2 is carboxamido, and R^5 is heteroaryl. By replacing the variables in formula **1** with the suggested values, and using quinoline as the heteroaryl, the following structure is obtained:



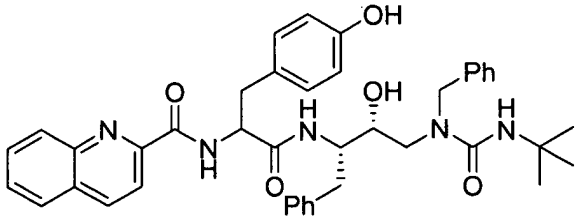
By contrast, compounds 7a, 7b, and 7c of the Kick *et al.* reference are:



7a



7b



7c

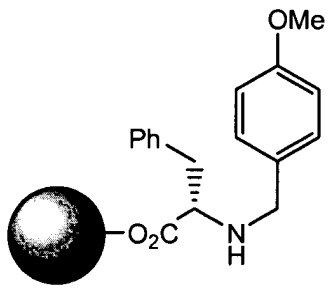
For the above reasons, the Office Action has not established that the present claims are anticipated by or obvious in view of the Kick *et al.* reference. Withdrawal of the corresponding rejections under 35 U.S.C. § 102 (b) and 35 U.S.C. § 103 (a) is respectfully requested.

Rejection under 35 U.S.C. §102 (b)/§103 (a) re Gordon *et al.*

The Examiner rejects claims 12, 18-21, 29, 35-39, 43, and 44 under 35 U.S.C. § 102 (b) as anticipated by, or, in the alternative, under 35 U.S.C. § 103 (a) as obvious over Gordon *et al.*, Bioorganic & Medicinal Chemistry Letters, 1995, Vol. 5, No. 1, 47-50. The Office Action alleges that the Gordon *et al.* reference discloses collections of compounds that read directly on the alpha amino acids in the claimed combinatorial library.

The Gordon *et al.* reference teaches reductive alkylation on a solid phase to form particular substituted amino acids which are subsequently converted to dipeptides and cyclized to form a piperazinedione combinatorial library.

The amino acids taught by the Gordon *et al.* reference (see, for example, formulas 1-4, page 47 and 6-8 on page 49) are bound to a solid substrate through their $-CO_2$ group, e.g., as shown in compound 3.

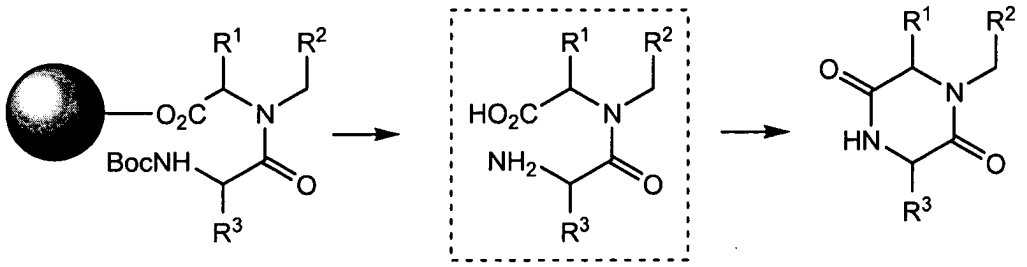


3

By contrast, the present combinatorial library requires that when the compounds are in an array having each compound located at a different position at a substrate, at least one of the compounds is coupled to the substrate through R^1 or R^2. The values claimed for R^1 and R^2 do not permit a carboxy substituted alkyl which would be needed to form the compounds of the Gordon *et al.* reference. Moreover, the claimed combinatorial library does not recite substituted oxycarbonyl groups for nitrogen taught by the Gordon *et al.* reference such as the Boc group in compounds 4 and 8 and the Fmoc group in compound 6.

The Gordon *et al.* reference teaches that compounds of formula 8 were Boc-deprotected with concomitant resin cleavage followed by a short reflux of the evaporated filtrate in toluene to induce cyclization to afford mixtures containing piperazinediones of formula 9 (see scheme 3,

page 49, and page 48, lines 15-17). The step of Boc-deprotection with concomitant resin cleavage suggests that mixtures of dipeptide intermediates are formed prior to cyclization:



8 **9**

Such dipeptide intermediates require both–NH_2 and -CO_2 groups. However, the claimed groups for R^1 and R^2 in formula **1** are not themselves permitted to be substituted with amino, let alone be a group such as -$C(=O)CH(R^3)NH_2$. Also, the claimed groups for R^1-R^5 are not themselves permitted to be substituted with carboxyl, let alone be a group such as -$CH(R^1)CO_2$. Consequently, the mixtures of cleaved dipeptide intermediates produced by the Gordon *et al.* reference do not anticipate the claimed combinatorial library.

Therefore, the Gordon *et al.* reference does not anticipate or obviate the claimed invention. Withdrawal of the corresponding rejections under 35 U.S.C. § 102 (b) and 35 U.S.C. § 103 (a) is respectfully requested.

Rejection under 35 U.S.C. § 112

The Examiner rejects claims 12, 18-21, 29, 35-39, 43, and 44 under 35 U.S.C. § 112, second paragraph as being indefinite. The Examiner states that there is uncertain antecedent basis for the term "the compound" in the last line of claims 12 and 44. Because Applicants have canceled claim 44 and deleted the last line from claim 12, the rejection is moot. Withdrawal of the rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

Conclusion

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested. Allowance of the claims remaining in this application is earnestly solicited.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5078.

Enclosed is a $60 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: March 2, 2006

Kraig K. Anderson
Reg. No. 54,961

Fish & Richardson P.C.
500 Arguello Street, Suite 500
Redwood City, California 94063
Telephone: (650) 839-5070
Facsimile: (650) 839-5071

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